

Outcome, comorbidity and prognosis in anorexia nervosa

Gabriela Jagielska¹, Iwona Kacperska²

¹ Department of Child Psychiatry, Medical University of Warsaw

² Child and Adolescent Psychiatry, Independent Public Children's Clinical Hospital in Warsaw

Summary

Anorexia nervosa (AN) is a relatively common disorder, especially in adolescent and young adult women. The lifetime prevalence of AN in females ranges from 1.2 to 2.2%. The prevalence in males is 10-times lower. The condition is associated with a high risk of chronic course and poor prognosis in terms of treatment and the risk of death. Longer follow-up periods seemed to correspond with increased improvement rates and increased mortality. Onset of the disorder during adolescence is associated with better prognosis. It is reported that as much as 70% to over 80% of patients in this age group achieve remission. Worse outcomes are observed in patients who required hospitalization and in adults. Recent studies indicate improved prognosis for cure and lower mortality rates than previously reported. However, the recovery can take several years and AN is associated with high risk of developing other psychiatric disorders during the patients' lifetime, even after recovery from AN (mainly: affective disorders, anxiety disorders, obsessive-compulsive disorders, substance abuse disorders). Studies indicate that bulimic symptoms often occur in the course of anorexia nervosa (especially within 2–3 years from the onset of AN). The authors present a review of literature on the course, comorbidity, mortality, and prognostic factors in AN. Better knowledge of the course of anorexia can contribute to more realistic expectations of the pace of symptomatic improvement, as well as to a creation of therapeutic programs which are better adapted to the needs of the patients.

Key words: anorexia nervosa, treatment outcome, mortality

Introduction

According to large population-based studies, the lifetime prevalence of anorexia nervosa (AN) in females ranges from 1.2 to 2.2% and that of sub-threshold/atypical AN (aAN) from 2.4 to 4.3% [1–3]. The estimated prevalence in males is 10-times lower [4], however, there are studies indicating the prevalence of AN in the male population to be somewhat higher. Bulik et al. [1] reported the prevalence of AN (according to DSM-IV criteria) in females to be 1.2%, and in males 0.29%, and according to DSM-

5 criteria AN prevalence in the population of 14-year-olds was estimated at 3.2% in females, and 1.6% in males [5].

The onset of AN most commonly occurs during adolescence, with 15–19-year-olds constituting 40% of newly diagnosed cases. Peak incidence is between 14 and 18 years of age. Approximately 85% of cases begin before the age of 20, and nearly all of them before the age of 25 [6]. AN is relatively rare in the population under 13 years of age [4]. Some studies indicate increasing incidence of AN [7–9], especially in females aged 15–24 years [8]. A meta-analysis of studies on AN incidence in Northern Europe indicates an increasing AN incidence until the 1970s, with a subsequent plateau at approximately 5–5.4 cases per 100,000 [8].

AN is a psychiatric disorder with a substantial comorbidity, chronic course, and the highest mortality among all psychiatric conditions [10]. The disorder presents a challenge for doctors and therapists as AN sufferers often deny being affected, hide their symptoms and signs, or avoid treatment. Studies demonstrate that only approximately 50% of AN cases are diagnosed [2] and only 1 in 3 of those diagnosed receive specialist care [11]. Out of those who begin treatment, 20–51% of inpatients and 23–73% of outpatients avoid or drop out from their treatment program [12].

Better knowledge of the course of anorexia can contribute to more realistic expectations of the pace of symptomatic improvement, as well as to a creation of therapeutic programs which are better adapted to the needs of the patients.

The course of anorexia nervosa

A meta-analysis of 119 studies published in the second half of the 20th century [13] demonstrated that $46.9 \pm 19.7\%$ of patients (range: 0–92%) recovered, $33.5 \pm 17.8\%$ of patients (range: 0–75%) improved, and $20.8 \pm 12.8\%$ of patients (range: 0–79%) suffered from chronic AN. Such considerable differences in the course of this condition are mostly due to variations in terms of the adopted recovery criteria, follow-up duration, duration of symptomatic remission, study group clinical characteristics, and the type of management. Longer follow-up periods seemed to correspond with increased improvement rates (and increased mortality). Follow-up durations of <4 years, 4–10 years, and >10 years corresponded to the recovery rates of $32.6 \pm 24.3\%$, $47 \pm 15.7\%$, and $73.2 \pm 16.2\%$, respectively.

Long-term treatment outcomes are better when considered with respect to the particular AN symptom normalization. For example, normalization of weight, menses, and eating habits were observed in $59.6 \pm 15.3\%$, $57.0 \pm 17.2\%$, and $46.8 \pm 19.6\%$ of cases, respectively [13]. A study in a group of adolescents receiving family therapy, with a 2–6-year-long follow-up, demonstrated that the rates of somatic recovery (defined as reaching >85% of ideal body weight – IBW) and resumption of menses were significantly higher than those of psychological recovery (94.4%, 90.5%, and 57.1%, respectively). In this study, the time necessary to reach weight improvement was less than 1 year and psychological remission was achieved after another year [14].

The course of anorexia nervosa in population-based studies

Based on the suppositions that patients requiring inpatient treatment may have poorer prognosis and that some patients would never begin therapy, some studies were conducted to assess the course of AN in groups comprising individuals selected from the general population. One of such studies compared adolescents (aged up to 19 years) selected during a population-based study (20% of whom had never had any contact with a psychiatrist and only 61% of whom had ever received therapy) and a control group of healthy adolescents. After 18 years of follow-up, 54% of individuals from the study group (vs. 88% of the control group) were free from disturbed behaviors and attitudes with respect to food and shape, while 22% (vs. 2% of the control group) avoided eating. According to the Morgan–Russell criteria, treatment outcomes were good, intermediate, and poor in 84%, 10%, and 6% of patients, respectively. Eighteen years after receiving AN diagnosis 12% of patients still met eating disorder criteria. AN persisted continually in 2% of patients [15].

In another group of females with the onset of AN during adolescence (57% of whom received specialist care at some point) weight normalization was observed in nearly all patients after 7 years, but in 41% of patients symptoms of eating disorder persisted (mainly bulimia nervosa – BN). After 10 years of follow-up, the study group did not differ from the control group in terms of body weight or BMI (Body Mass Index), while 27% of females still met eating disorder criteria. One third of patients reported running commentary voices with regards to eating-associated behaviors during the period of AN symptoms, and 11.8% of patients underwent a psychotic episode during follow-up. After a 10-year follow-up, Morgan–Russell’s good, intermediate, and poor outcome was exhibited by 49%, 41%, and 10% of patients, respectively. No deaths were reported during the study. The authors suggested that the outcome in the case of treated patients might be very similar to the natural outcome of the illness [16].

A population-based study in adolescent females [2] showed a symptomatic improvement in 66.8% of patients with AN and 69.1% of patients with atypical AN (aAN) within 5 years. The outcomes did not differ in the treated and untreated groups. Most patients achieved clinical improvement within 5 years and, from that point on, improvement usually progressed until full recovery. The endpoint of follow-up saw recovery in 70.9% of females with AN and in 76.6% of females with aAN. Five years after clinical improvement, most patients achieved complete, or nearly complete, psychological recovery (in Eating Disorders Inventory subscales – EDI) and their body weight approached that of their healthy peers.

Another, similar population-based study of AN outcome, that adopted a relatively high BMI criterion for good treatment outcome ($\text{BMI} \geq 19 \text{ kg/m}^2$), included adolescents and adults newly diagnosed at the level of primary healthcare. After an average of approximately 5 years, the study showed good treatment outcomes in 55% of patients with restrictive type AN and in 57% of patients with bulimic-type AN, while intermediate outcomes were observed in 21% and 17% of patients, respectively, and poor outcomes in 21% and 32%, respectively [17].

The course of anorexia nervosa depending on the age of patients

AN treatment outcomes observed in adult groups, jointly evaluated groups of adults and adolescents are worse than in adolescents [13, 18–21]. According to meta-analysis by Steinhausen [13], treatment outcomes in adolescents were better than those observed in the adolescent and adult populations evaluated jointly (with good treatment outcomes observed in $57.1 \pm 15\%$ vs. $44.2 \pm 21.8\%$ of those populations, respectively, and a chronic course observed in $16.9 \pm 7.5\%$ vs. $23.5 \pm 14.9\%$ of those populations, respectively). More recent studies in adolescents with AN indicate that approximately 70%, and even over 80% of adolescents achieve remission [13, 18–21].

A 10-year-long prospective study by Herpertz-Dahlmann et al. [19] in adolescent females hospitalized due to AN showed a complete recovery rate of 69%. Importantly, the patients with long time since their improvement did not differ from the control group in terms of other psychiatric disorders or psychosocial functioning. Another long-term observational study in women who had received (as adolescents) an average of 12 months of comprehensive therapy at a specialist facility, showed increased remission rates from 67.6% after 8 years to 85.3% after 16 years, with the achieved remissions seemingly permanent. Between year 8 and 16 of follow-up, the study also demonstrated a considerable improvement in the following symptoms: desire to be thin, body dissatisfaction and bulimic symptoms, while difficulties in recognizing emotions and in identifying hunger and satiety persisted [21]. A similarly good outcomes (remissions after 3.5–14.5 years in 82% of cases) were achieved in a group of adolescent females receiving intensive treatment involving brief periods of hospitalization (when strictly necessary); with almost all patients receiving further outpatient care [18].

In another long-term study (follow-up of 10–15 years after hospitalization) in a group of adolescent patients receiving intensive therapeutic program (including individual, group and family therapy) 75.8% of patients reached complete recovery, with a partial recovery rate of 10.5%, and chronic AN in 13.7%. Transient symptoms aggravation was observed in 30% of patients. Following recovery, AN recurrences were relatively rare. Patients with chronic AN demonstrated considerably poorer work adjustment, social relations, and life satisfaction after a period of 5 and 10 years in comparison with healthy individuals and those with partial improvement [22].

In one study AN outcomes and mortality were compared in three age groups (<18 years old, aged 18–39, and ≥ 40 years old). The study showed the poorest treatment outcome, social and interpersonal functioning, and quality of life in patients who were in the 18–39 age group at the beginning of the follow-up. This age group also showed the highest mortality [23].

Outcome of anorexia nervosa in hospitalized patients

Worse outcomes are observed in patients who required hospitalization.

A review of the literature from the period 2004–2009 showed that treatment outcomes ranged from optimistic for patients of community health clinic (2% of them continued to be diagnosed with AN after a 9-year follow-up), to much worse for

inpatients (18% of inpatients met AN criteria after 12 years of follow-up). Authors summarized that a majority of outpatients with AN are in remission five or more years following presentation and conversely, minority of patients with AN treated in inpatient settings achieve remission irrespective of whether follow-up occurs 2 or 12 years following hospitalization [24].

Sullivan et al. [25] reported that 10% of patients continued to meet criteria of AN 12 years after their first hospitalization, while 15.7% had aAN. The authors emphasized the fact that even females who did not meet the criteria of AN had a relatively low body weight, cognitive functioning characteristic of AN, and significantly lower desired BMI in comparison to those parameters in females from the control group. It should be emphasized that in the past the outcomes for hospitalized patients were worse than in the present.

Despite its average follow-up of 20 years, one study that evaluated patients (adolescents and adults with a relatively long duration of the illness and low body weight before hospitalization) hospitalized in the sixties showed generally poorer treatment outcomes with good treatment outcomes reported only in 30% of patients, intermediate outcomes in 32.5% of patients, and poor treatment outcomes in 20% of patients (17.5% of patients died) [26]. A more recent example of poor outcome of AN was a 21-year-long prospective study in adolescent and adult females following their first hospitalization that was published in 2000. This study showed complete recovery in 50.6% of patients, improvement in 20.8% of patients, and persistent fully symptomatic AN (according to DSM-IV criteria) in 10.4% of patients. The mortality rate was 16.7% [27].

After hospital discharge health deterioration is a common phenomenon in AN patients.

An observational study of patients treated in a hospital setting (undergoing intensive treatment) showed moderate or slight deterioration in their condition within the first two years after discharge with respect to the improvement achieved during hospitalization. However, progressive improvement was observed after 3–12 years of follow-up [28].

Another study demonstrated good outcomes (according to Morgan–Russell criteria) after an average of approximately 8 years follow-up in 75% of patients, intermediate outcomes in 11% of patients, and poor outcomes in 14% of patients treated during adolescence, despite frequent need for re-hospitalization (35% of the study group). However, 38% of patients were still concerned about their weight and appearance (including 62% who continued to limit their food intake) [29].

Chronic course of anorexia nervosa

A number of studies indicate that AN is a potentially chronic disorder both in the treated and the general populations. According to Strober et al. [22], patients with adolescent-onset AN who underwent intensive treatment required from 4.8 to 6.6 years to recover. The rates of partial and complete improvement 2 years after hospitalization were 10% and 0%, respectively, and 3 years after hospitalization – 21% and 1%, respectively. Improvement rate increased rapidly 4 years after hospital treatment.

Partial improvement or complete recovery after 5 years were observed in 54.8% and 17.9% of patients, respectively, and increased in the subsequent years of follow-up (to 73.7% and 58.9%, respectively, after 7 years, and to 84.3% and 72.6%, respectively, after 10 years). There were also sporadic cases of complete recovery after more than 10 years of follow-up.

The average duration of AN in patients identified in a population-based study of adolescents was 3.4 ± 2.4 years (range 0.9–14.7 years) [15]. Another, similar study in the general population showed that the median time to recovery for the restrictive type of AN was 3.3 years, and binge-eating/purging type of AN – 4.4 years [17]. Likewise, a study by Råstam et al. [16] showed the mean duration of symptoms to be 3.3 years (2.7–3.8 years).

Bulimic symptoms in the course of anorexia nervosa

Studies indicate that bulimic symptoms often occur in the course of anorexia nervosa. Strober et al. [22] demonstrated that approximately 30% of patients with restrictive type of AN exhibit binge-eating episodes (with an onset after an average of 24 months of follow-up). This symptom was more common in patients with a hostile attitude toward their families and in the case of absent parental empathy and tenderness toward the patient. Eckert et al. [30], who included only female patients hospitalized for AN, demonstrated that a period of bulimic symptoms occurred in up to 64% of cases. The high prevalence of bulimic symptoms in AN was also confirmed in a population-based study with an 18-year follow-up of adolescents (some of them treatment-naïve), which showed that only 24% of patients had never exhibited bulimic symptoms [15]. Another study showed 15% of patients exhibiting symptoms of BN after 20 years of follow-up [26].

Diagnostic crossover to BN among hospitalized adolescent and adult patients with AN (binge-eating/purging type in 71% of patients) occurred both in the restrictive type and binge-eating/purging type; however, in the longer perspective, this occurred in patients initially diagnosed with binge-eating/purging type. After 12 years of follow-up, crossover from AN to BN persisted only in 9.5% of patients [28].

According to a number of authors, symptoms of bulimia develop within 2–3 years from the onset of AN [16, 22, 25, 30, 31]. Sullivan et al. [25] reported diagnostic crossover from AN to BN mainly within the first 2 years of follow-up, while development of BN after 5 years from AN onset was considered unlikely. This study with an average of 12-year follow-up after the first hospitalization, showed that 54% of females met criteria for BN at some point. After 12 years, BN criteria were met by 11.4% of patients.

Contrary to the findings in the above-mentioned studies, a follow-up of patients undergoing comprehensive treatment, mainly in outpatient setting, demonstrated symptoms of bulimia in only 5% after 8 years and in 1.5% of patients after 16 years [21]. One population-based study showed no conversion to symptoms of bulimia in patients with a restrictive type of AN (diagnosed in primary care setting) [17].

Mortality in anorexia nervosa

Mortality in AN depends on study group characteristics (general vs. hospitalized population, disorder severity, diagnostic criteria), sample size, follow-up duration, separate analysis of AN and other eating disorders, and the type of therapy.

Reported crude death rates (the proportion of deaths in a given population) range from 0 to 22.5%, while the standardized mortality ratio (SMR), which quantifies the increase in mortality in a study population of the same age, ranges from 0 to 17.8. The SMR for suicidal death in AN ranges from 23.1 to 56.9 (as cited in: [32]). According to Klump et al. [10] the SMR in AN is the highest of that in all psychiatric disorders.

Patients who receive treatment during adolescence are at a lower risk of death. Some studies even suggest no mortality after 10 years of follow-up in patients with adolescent-onset AN [18, 19, 22, 33]. Moreover, after 10–15 years of follow-up, no deaths were observed in patients receiving intensive therapeutic support and nutritional treatment in a hospital setting [22] as well as during an 18-year-long prospective observational study in patients with AN identified in screening tests of adolescents aged up to 19 years (despite the fact that most of the patients did not receive therapy and 20% of patients did not receive specialist care) [15].

The crude death rate in a prospective long-term population-based study in Finnish teenagers, including also untreated cases, was 0.3% per decade [2]. Another population-based study in cases of AN newly diagnosed in primary care setting (an average follow-up of 5 years) reported a 0.7% mortality [17].

An analysis of national Swedish registry including female patients undergoing treatment during adolescence in the period between 1987 and 1993 demonstrated total mortality of 1.2%, and AN-related mortality of 0.8%. The SMR was 3 [34]. A similar low mortality (1%) was observed in a group of patients treated during adolescence (receiving intensive comprehensive therapy) [21].

Worse outcomes with higher mortality were observed in groups of adults, jointly analyzed adults and adolescents, and patients requiring treatment in a hospital setting. For example, after an average of 8-year follow-up, in the group of outpatient females who were adolescents or adults at the time of qualification for treatment, the mortality rate was 4.27%, and after excluding non-AN-related deaths SMR was 9.7. A meta-analysis (including 2,240 patients) conducted by the same authors showed that the mortality rate in AN was 5.25% and the SMR was 9.7 [35].

A prospective study in adolescents and adults requiring hospitalization (binge-eating/purging type of AN constituted 71%) showed crude death rate of 4.9% after 2 years, 5.8% after 6 years, and 6.8% after 12 years. The SMR after 12 years was 8.85. The patients who died had exhibited higher rates of depression, lower body weight, higher rates of laxative abuse, hypersensitivity in social relations, feeling of inadequacy, higher rates of introversion, lower self-esteem, and poorer social functioning at the time of hospital admission [28].

Long-term treatment outcomes of other studies on the results of treatment in severe cases from tertiary centers or those hospitalized showed high crude death rates of up

to 16–18% [15, 26, 27, 36]. For example, one prospective study (average follow-up of 21 years after the first hospitalization) reported an AN-related mortality of 15.6% [27]. The SMR in a large cohort study in patients admitted to tertiary hospitals (treated in the 80s and in the 90s) was as high as 10.5 (with 41% of deaths being due to suicides) [37].

A meta-analysis of 42 studies (average follow-up of 7.6 years – from 1.7 to 33 years, 3,006 subjects) demonstrated crude death rate in AN of 5.9% (0.56% per year and approximately 5.6% per decade). The SMR in females with AN aged 15–24 was 12 and was two times higher than that in the group of females hospitalized for other psychiatric reasons. The causes of death were: AN complications, suicides, and unknown in 54%, 27%, and 19% of cases, respectively. The suicide rates were 200-times greater than those in the general population [38].

A more recent meta-analysis of studies published in the second half of the 20th century (5,590 patients) yielded a crude death rate of 5.9±5.7% (range 0–22%). The mortality rate was 0.9%±2% in the follow-up period of <4 years, 4.9%±4.3% in the follow-up period of 4–10 years, and 9.4%±8.3% in the follow-up period of >10 years. The SMR ranged from 1.36 to 17.8. The highest SMR value (30) was observed within the first year after presentation. The mortality rate in patients treated during adolescence were lower than those in studies where adolescents and adults were evaluated jointly (1.8%±2.5% and 5.9%±5.7%, respectively) [13].

A meta-analysis of studies published between the year 1996 and 2010 (12,189 patients) indicated that the SMR for AN patients was 5.85. The higher mortality rates were associated with age, low BMI, comorbidities (affective disorders, history of suicidal and self-harm behaviors, alcohol abuse) and hospitalization due to other psychiatric disorders. Few deaths were reported in the younger age group, while many deaths were reported in those treated at the age of 20 and over. The SMR values in the youngest patients (age at hospitalization 15–19 years), in those hospitalized at 20–29, and in those treated at age 30 and over were 3, 10, and 6, respectively [39].

Analysis of 6,009 females hospitalized due to AN at least once in relation to the cause of death registry in Sweden revealed high SMRs (the SMR for all causes 6.20, with the SMRs for natural and unnatural causes 4.9 and 8.9, respectively). The highest SMR (of 650.0) was for AN-related deaths, followed by the SMRs for substance abuse (18.9) and suicide (13.6). The patients who were older at the time of hospitalization were at a higher risk of early death (twofold higher in those aged 20–29 years and fourfold higher in those aged 30–39 years in comparison to that for the age 10–19) and underwent repeated hospitalizations including psychiatric hospitalizations for other disorders. Authors emphasized that recent years have seen a decrease in the reported mortality rates, which may be associated with improved care and therapy, treatment of psychiatric comorbidities, better realimentation strategies, and a better control of somatic disorders [32].

The recent findings of lower mortality rates were confirmed by an analysis of studies published between 2004 and 2009. In this period, the crude death rate ranged from 0 to 8%, with the cumulative death rate of 2.8% [24].

Comorbidities in anorexia nervosa

AN is associated with a high comorbidity. Micali et al. [5] indicated that comorbidity is a common problem during the acute phase of the illness. A 2-year follow-up of adolescents aged 14 and 16 meeting the DSM-5 criteria for AN showed an increased risk of depressive and anxiety disorders. Many studies show a high risk of developing other psychiatric disorders during the patients' lifetime, even after recovery from AN. Additional psychiatric disorders are more likely to occur in those still affected. Two thirds of patients with a persistent eating disorder and one third of those who stopped meeting eating disorder criteria had at least one other psychiatric disorder [18].

A meta-analysis of studies published in the second half of the 20th century [13] indicated that affective disorders occurred in 24.1%±16.3% (2–67%), neurotic or anxiety disorders in 25.5%±14.9% (4–61%), obsessive-compulsive disorders in 12%±6.4% (0–23%), substance abuse disorder in 14.6%±10.4% (2–38%), and schizophrenia in 4.6%±5.7% (1–28%) of AN patients. A follow-up in patients with AN showed concomitant partially or fully symptomatic eating disorders or another psychiatric disorder without eating disorders in over 50% of patients. A total of 31%±25.1% (0–76%) of patients had an obsessive-compulsive personality disorder, 16.6%±19.9% (0–53%) of patients had a histrionic personality disorder, and 17.4%±16.8% (0–69%) of patients had other personality disorders including borderline states.

A 12-year follow-up of AN patients by Sullivan et al. [25] showed higher rates of various psychiatric disorders during their lifetime versus the control group (respectively: depression disorders in 51.4% and 35.7%; alcohol dependence in 27.1% and 10.2%; other dependencies in 30% and 12.2%; anxiety disorders in 60% and 32.7%). The following disorders were significantly more common in the affected group than in the control group: generalized anxiety disorder, separation anxiety disorder, obsessive-compulsive disorder, and panic disorder. An 18-year follow-up of patients with adolescent-onset AN versus the control group also showed the proportion of patients with at least one additional psychiatric disorder to be over two times higher than in the control group (39% vs. 16%, respectively) [18].

Sixteen years after the beginning of treatment (when 85.3% of patients no longer had AN symptoms and 68% of patients — no eating disorders) 37% of patients continued to have symptoms of various psychiatric disorders (which did not disturb the patients' functioning in most cases), including most frequently symptoms of depression (56%), anxiety disorders (28%), and obsessive-compulsive disorders (12%) [21].

Another study with good treatment results (82% of patients in remission) after a 3.5–14.5-year follow-up showed at least one axis I psychiatric disorder (according to DSM-IV) in 41% of patients (most commonly a depressive or anxiety disorder), with 10% of patients exhibiting symptoms of post-traumatic stress disorder (PTSD). At the end of the follow-up period, 55% of patients exhibited eating disorders or other psychiatric disorders [18].

Additional psychiatric disorders are more common in patients with binge-eating/purging subtype of AN. Fichter et al. [28] conducted a 12-year follow-up of adoles-

cents and adults with a history of hospital treatment, including a high rate of patients with binge-eating/purging type of AN. The study showed the presence of psychiatric disorders in as many as 76.6% of patients. The respective lifetime prevalence and end-of-follow-up rates for mood disorders were 63.8% and 20.8%, major depression – 54.4% and 16.9%, dysthymia – 9.1% and 3.9%, anxiety disorders – 46.3% and 28.6%, panic attacks – 20.8% and 11.7%, obsessive-compulsive disorder – 18.2% and 13%, substance use disorders – 29.9% and 9.1%, drug dependence (mostly involving prescription drugs) – 16.9% and 2.6%, and psychotic disorders – 1.3% and 0%. Borderline personality was observed in 9.1% of patients (the article does not state at which point of observation).

A 9–14-year follow-up conducted in females born between 1968 and 1977 (in Sweden) and hospitalized during adolescence due to AN showed that 8.7% of them had persistent chronic psychiatric problems requiring inpatient treatment, while 21.4% of them received social welfare. These patients had a 5.8-fold higher risk of poor health (requirement for psychiatric hospitalization and/or death), and a 2.6-fold higher risk of welfare dependency than that in the general population [34].

Råstam et al. [16] emphasized the fact that approximately 50% of patients suffered from premorbid symptoms of obsessive-compulsive disorder (OCD), particularly, obsessive-compulsive personality disorder (OCPD) and that depressive symptoms usually develop during the course of AN. Over one third of patients were diagnosed with OCD within their lifetime. After 7 years of follow-up in females with adolescent-onset AN (after almost all patients achieved weight normalization) affective disorders, OCD, and avoidant personality disorder continued to be overrepresented, and one in five patients exhibited an autism spectrum disorder (ASD). After 10 years, the rates of ASD or OCPD were over two times higher than in the control group, with affective disorders (particularly depression and dysthymia) and anxiety disorders (particularly OCD) more common than in the control group. Some authors go as far as to believe that AN is a particular type of OCD, however, obsessions and compulsions are most commonly associated with eating, appearance, and compulsive physical exercises, although the content and severity of symptoms allow to establish an additional diagnosis only in some patients (as cited in: [40]).

Polish study in a large group of females treated in a hospital setting confirmed high rates of OCD symptoms (in 25% of patients), with none of the patients meeting the diagnostic criteria of OCD. Most of the patients reported the effect of OCD symptoms on their functioning as low [41].

Prognostic factors

A meta-analysis of studies published in the second half of the 20th century [13] showed that self-induced vomiting, purgative abuse, bulimic type of AN, chronic character of symptoms, and obsessive-compulsive personality were associated with poorer prognosis, whereas histrionic personality was associated with better outcomes. The analysis was inconclusive as to the effect of the duration of inpatients treatment or the degree of weight loss. Hyperactivity was found to have no prognostic significance.

A review of literature from the period 2004–2009 suggested that symptom severity with the necessity for inpatient treatment and illness duration before treatment initiation can help predict poorer treatment outcomes [24]. A number of studies indicated that the outcomes in terms of mortality, psychosocial functioning, psychiatric disorders, and eating-related problem behaviors were better in adolescent-onset AN than in adult-onset AN [20, 22, 42, 43]. Poor prognosis was reported in patients with a very early illness onset (age 8–14) [44]. A more favorable prognosis in patients with adolescent-onset AN and a poor prognosis in patients with childhood-onset AN were confirmed in a meta-analysis by Steinhausen [13]. The meta-analysis also indicated that a good parent-child relationship may protect against an unfavorable outcome. A large population-based study (including some treatment-naïve patients) showed a higher recovery rate in patients diagnosed before age 19 than in those ≥ 20 years old [17].

Favorable predictors in AN include early treatment initiation and good social adjustment in the period prior to AN onset (as cited in: [45]). According to a study by Wentz et al. [15] obsessive-compulsive personality traits preceding the onset of AN, age of onset, and premorbid autistic traits are unfavorable prognostic factors in the group of patients with adolescent-onset AN. Råstam, Gilberg and Wentz [16] reported that concomitant OCD, OCPD, and ASD have a negative effect on AN outcome. Błachno et al. [41] demonstrated that the presence of OCD symptoms was associated with the risk of more rapid weight loss and a longer period necessary for weight restoration.

Strober et al. [22] indicated a greater likelihood of a chronic course of the illness in patients with exacerbated compulsive exercising toward the end of hospitalization and poor social relations prior to illness onset. A longer time to recovery was observed in patients with a hostile attitude toward their families and very severe compulsive behaviors in everyday activities. Early illness onset (before the age of 12) in this study was not found to be associated with prediction of complete or partial recovery. Older age at the beginning of follow-up, alcohol or drug abuse, endocrine disorders, negative family history for eating disorders were shown to be predictors of poor outcomes or death [23].

Tozzi et al. [46] presented an interesting approach to factors associated with recovery and persistent AN symptoms. After an average of 15 years of AN onset (during adolescence and adulthood), the most common patient-reported factors contributing to recovery were supportive nonfamilial relationship or having a partner, maturation or growing out of the illness, therapy or counseling, while the factors contributing to persistent illness were the family's focus on their weight and eating as well as their own low self-esteem.

Conclusions

Despite the fact that recent studies report improved outcome for patients with anorexia nervosa, it remains a serious disorder associated with high risk of chronic course and death. More favorable outcome is observed in adolescent population.

The need for longstanding follow up and frequent psychiatric comorbidity should be considered in treatment of anorexia nervosa.

Future studies should focus on evaluation of different therapeutic programs, which may further improve the effectiveness of treatment of AN.

References

1. Bulik CM, Sullivan PF, Tozzi F, Furberg H, Lichtenstein P, Pedersen NL. *Prevalence, heritability, and prospective risk factors for anorexia nervosa*. Arch. Gen. Psychiat. 2006; 63(3): 305–312.
2. Keski-Rakhonen A, Hoek HW, Susser ES, Linna MS, Sihvola E, Raevuori A et al. *Epidemiology and course of anorexia nervosa in the community*. Am. J. Psychiat. 2007; 164: 1259–1265.
3. Wade TD, Bergin JL, Tiggemann M, Bulik CM, Fairburn CG. *Prevalence and long-term course of lifetime eating disorders in an adult Australian twin cohort*. Aust. NZ J. Psychiat. 2006; 40(2): 121–128.
4. Smink FRE, Hoeken D van, Hoek RW. *Epidemiology of eating disorders: Incidence, prevalence and mortality rates*. Curr. Psychiat. Rep. 2012; 14: 406–414.
5. Micali N, Solmi F, Horton NJ, Crossby RD, Edyy KT, Calza JP et al. *Adolescent eating disorders predict psychiatric, high-risk behaviours and weight outcome in young adulthood*. J. Am. Acad. Child Psych. 2015; 54(8): 652–659.
6. Herpertz-Dahlmann B. *Adolescent eating disorders: definitions, symptomatology, epidemiology and comorbidity*. Child Adol. Psych. Cl. 2008; 18: 31–47.
7. Lukas AR, Beard CM, O’Fallon WM, Kurland LT. *50-year trends in the incidence of anorexia nervosa in Rochester, Minn.: a population-based study*. Am. J. Psychiat. 1991; 148: 917–922.
8. Hoek HW. *Incidence, prevalence and mortality of anorexia nervosa and other eating disorders*. Curr. Opin. Psychiat. 2006; 19(4): 389–394.
9. Son GE van, Hoeken D van, Bertelds A, Furth EF van, Hoek HW. *Time trends in the incidence of eating disorders: a primary care study in Netherlands*. Int. J. Eat. Disorder 2006; 39: 565–569.
10. Klump KL, Bulik CM, Kaye WH, Treasure J, Tyson E. *Academy for eating disorders position paper: eating disorders are serious mental illnesses*. Int. J. Eat. Disorder 2009; 42(2): 97–103.
11. Hoek HW, Hoeken D van. *Review of the prevalence and incidence of eating disorders*. Int. J. Eat. Disorder. 2003; 34: 383–396.
12. Abbate-Daga G, Amianto F, Delsedime N, De-Bacco C, Fassino S. *Resistance to treatment and change in anorexia nervosa: a clinical overview*. BMC Psychiatry 2013; 13: 294–312.
13. Steinhausen HCh. *The outcome of anorexia nervosa in the 20th century*. Am. J. Psychiat. 2002; 159: 1284–1293.
14. Couturier J, Lock J. *What is recovery in adolescent anorexia nervosa*. Int. J. Eat. Disorder 2006; 39(7): 550–555.
15. Wentz E, Gillberg IC, Anckarsäter H, Gillberg CH, Råstam M. *Adolescent-onset anorexia nervosa: 18-year outcome*. Brit. J. Psychiat. 2009; 194: 168–174.
16. Råstam M, Gillberg C, Wentz E. *Outcome of teenage-onset anorexia nervosa in a Swedish community-based sample*. Eur. Child Adoles. Psych. 2003; 12(Suppl. 1): 178–190.
17. Son GE van, Hoeken D van, Furth EF van, Donker GA, Hoek HW. *Course and outcome of eating disorders in a primary care-based cohort*. Int. J. Eat. Disorder 2010; 43: 130–138.
18. Halvorsen I, Andersen A, Heyerdahl S. *Good outcome of adolescent onset anorexia nervosa after systematic treatment*. Eur. Child Adoles. Psych. 2004; 13: 295–306.

19. Herpertz-Dahlmann B, Müller B, Herpertz S, Heussen N, Hebebrand J, Remschmidt H. *Prospective 10-year follow-up in adolescent anorexia nervosa-course, outcome, psychiatric comorbidity and psychosocial adaptation*. J. Child Psychol. Psychiatry 2001 Jul;42(5): 603-612.
20. Steinhausen HC, Boyadjieva S, Grigorieu-Serbanescu M, Neumärker KJ. *The outcome of adolescent eating disorders, finding from an international collaborative study*. Eur. Child Adolesc. Psych. 2003; 12: 91-98.
21. Nilsson K, Hägglöf B. *Long-term follow-up of adolescent onset anorexia nervosa in Northern Sweden*. Eur. Eat. Disord. Rev. 2005; 13: 89-100.
22. Strober M, Freeman R, Morrell W. *The long-term course of severe anorexia nervosa in adolescents; Survival analysis of recovery, relapse, and outcome predictors over 10-15 years in a prospective study*. Int. J. Eat. Disorder 1997; 22(4): 339-360.
23. Ackard DM, Richter S, Egan A, Cronemeyer C. *Poor outcome and death among youth, young adults, and midlife adults with eating disorders: an investigation of risk factors by age AT assessment*. Int. J. Eat. Disorder 2014; 47(7): 825-835.
24. Keel PK, Brown TA. *Update on course and outcome in eating disorders*. Int. J. Eat. Disorder 2010; 43: 195-204.
25. Sullivan PF, Bulik CM, Fear JL, Pickering A. *Outcome of anorexia nervosa: a case-control study*. Am. J. Psychiat. 1998; 155(7): 939-946.
26. Ratnasuryia RH, Eisler I, Szmukler GI, Russell GF. *Anorexia nervosa: outcome and prognostic factors after 20 years*. Brit. J. Psychiat. 1991; 158: 495-502.
27. Zipfel S, Löwe B, Reas DL, Deter H-CH, Herzog W. *Long-term prognosis in anorexia nervosa: lessons from 21-year follow-up study*. Lancet 2000; 355: 721-722.
28. Fichter MM, Quadflieg N, Hedlund S. *Twelve-year course and outcome predictors of anorexia nervosa*. Int. J. Eat. Disorder 2006; 39: 87-100.
29. Komender J, Popielarska A, Tomaszewicz-Libudziec C, Jagielska G, Brzozowska A, Wolańczyk T. *Odległe wyniki leczenia dorastających chorych na jadłowstręt psychiczny*. Psychiatr. Pol. 1998; 32(6): 759-769.
30. Eckert ED, Halmi KA, March P, Grove W, Crosby R. *Ten-year follow-up of anorexia nervosa: clinical course and outcome*. Psychol. Med. 1995; 25(1): 143-156.
31. Bulik CM. *Eating disorders in adolescents and young adults*. Child Adol. Psych. Cl. 2002; 11: 201-218.
32. Papadopoulous FS, Ekblom, Brandt L, Ekselius L. *Excess mortality, causes of death and prognostic factors in anorexia nervosa*. Brit. J. Psychiat. 2009; 194: 10-17.
33. Wentz E, Nilsson E, Gillberg C, Gillberg IC, Råstam M. *Ten-year follow-up of adolescent-onset anorexia nervosa: psychiatric disorders and overall functioning scales*. J. Child Psychol. Psych. 2001; 42(5): 613-622.
34. Hjern A, Lindberg L, Lindblad F. *Outcome and prognostic factors for adolescent female inpatients with anorexia nervosa: 9 - to 14-year follow-up*. Brit. J. Psychiat. 2006; 189: 428-432.
35. Signorini A, De Filippo E, Panico S, De Caprio C, Pisanisi F, Contaldo F. *Long-term mortality in anorexia nervosa: a report after 8-year follow-up and review of the most recent literature*. Eur. J. Clin. Nutr. 2007; 61: 119-122.
36. Theander S. *Outcome and prognosis in anorexia nervosa and bulimia: some results of previous investigations, compared with those of a Swedish long-term study*. J. Psychiatr. Res. 1985; 19: 493-508.
37. Birmingham CL, Su J, Hlynsky JA, Goldner EM, Gao M. *The mortality rate from anorexia nervosa*. Int. J. Eat. Disorder 2005; 38: 143-146.

38. Sullivan PF. *Mortality in anorexia nervosa*. Am. J. Psychiat. 1995; 152: 1073–1074.
39. Arcelus JA, Mitchell AJ, Wales J, Nielsen S. *Mortality rates in patients with anorexia nervosa and other eating disorders: a meta-analysis of 36 studies*. Arch. Gen. Psychiat. 2011; 68(7): 724–731.
40. Błachno M, Bryńska A. *Comorbidity and characteristic of obsessive-compulsive symptoms in anorexia nervosa*. Psychiatr. Pol. 2012; 46(6): 1019–1028.
41. Błachno M, Bryńska A, Tomaszewicz-Libudzić C, Jagielska G, Srebnicki T, Wolańczyk T. *The influence of obsessive compulsive symptoms on the course of anorexia nervosa*. Psychiatr. Pol. 2014; 48(3): 429–439.
42. Hsu LKC. *Outcome and early onset anorexia nervosa. What do we know?* J. Youth Adolesc. 1996; 25: 563–568.
43. Theander S. *Anorexia nervosa with early onset: Selection, gender, outcome, and results of longterm follow-up study*. J. Youth Adolescence 1996; 25: 419–430.
44. Lask B, Bryant-Waugh B. *Early-onset anorexia nervosa and related eating disorders*. J. Child Psychol. Psychiat. 1992; 33: 281–300.
45. Cygankiewicz P, Solecka D, Pilecki MW, Józefik B. *Predyktory poprawy objawowej w zaburzeniach odżywiania się. Analiza wstępna*. Psychiatr. Pol. 2012; 46(2): 201–212.
46. Tozzi F, Sullivan PF, Fear JL, McKenzie J, Bulik CM. *Causes and recovery in anorexia nervosa: the patient's perspective*. Int. J. Eat. Disorder 2003; 33: 143–154.

Address: Gabriela Jagielska
Department of Child Psychiatry
Medical University of Warsaw
02-691 Warszawa, Żwirki i Wigury Street 63A